

Spending on Antineoplastic Agents in the United States, 2011-2016

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- **Table 2 is to be published online only** (Top 25 Injectable Drugs & Biologics by Expenditure in Clinics and Hospitals in 2015-2016 and Percent Change from 2015)

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Samuel J. Hong consulted for Astellas Pharma.

Edward C. Li has received honoraria for speaking on behalf of Pfizer, and for serving on advisory boards for Eli Lilly, Pfizer, Heron Therapeutics, Mylan, Taiho, and Sandoz. He is currently an employee of Sandoz.

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Samuel J. Hong, Edward C. Li, Glen T. Schumock

Introduction

Recent cancer drug approvals are lauded as being more effective with relatively fewer adverse effects, but these treatments come with a great cost to the United States (US) health care system.¹ There is little information on recent trends in actual antineoplastic expenditures representative of the whole US healthcare system or by sector. Therefore, the objective of this study was to describe antineoplastic expenditures in the US by year and sector.

Methods: This was a retrospective, cross-sectional study of IQVIA (formerly QuintilesIMS) National Sales Perspective data for the period of January 1, 2011, to December 31, 2016. Actual expenditures were totaled by healthcare sector and calendar year, then adjusted for medical-cost inflation to 2016 dollars. Growth was calculated as the percentage increase from the previous year.

Results: Total expenditures of antineoplastic agents across all channels grew from \$26.8 billion in 2011 to \$42.1 billion in 2016. Antineoplastic spending increased 12.2% in 2016 (compared to the previous year), followed by 15.6% in 2015, 13.4% in 2014, 6.3% in 2013 and 0.4% in 2012. Throughout the study period, 96.5% of total

antineoplastic expenditures occurred within clinics, mail-order pharmacies, non-federal hospitals, and retail pharmacies.

Conclusion: Antineoplastic expenditures are expected to increase due to continuing development and approval of costly targeted cancer therapies. Cost containment and utilization management strategies must be balanced so as not to restrict access or disrupt innovation. Future policies should focus on ensuring safe and appropriate use of antineoplastics while balancing long term drug costs.

INTRODUCTION:

The United States has made noteworthy progress in the care of patients with cancer, as evidenced by the significant declines in cancer related mortality for the most common cancers.² These meaningful and durable improvements in cancer outcomes have been in part attributed to the development of new drugs and technologies.¹ Between 2011-2016, the US Food and Drug Administration approved 52 new cancer therapies.³⁻⁸ Additionally, the oncology drug pipeline grew by 45% over the last decade and there are 631 unique molecules in late phase development.^{9,10} Cancer research is likely to continue or even accelerate with the recent enactment of the 21st Century Cures Act. This legislation increases funding for medical research, and includes the Beau Biden Cancer Moonshot Initiative, which is likely to serve as a catalyst for the approval of new cancer therapies.¹¹⁻¹³ In addition, many new treatments have received expanded indications after the initial approval. For example, the US Food and Drug Administration (FDA) has approved pembrolizumab for microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) tumors, marking the first time the FDA approved a cancer treatment based on a common biomarker instead of the location of the tumor origin.¹⁴

However, these new cancer therapies come with significant financial consequences. Since the year 2000, there has been an upward trajectory in the monthly costs of cancer therapies and from 2011 to 2016, oncology was ranked the highest therapeutic area in specialty drug spend.^{9,15,16} According to an analysis in 2015, antineoplastic drug prices

have risen faster than those for other therapeutic areas, and the median price per year of therapy for new drugs approved between 2009 and 2013 was \$115,981.¹⁷ With an increasingly robust oncology pipeline and improving survival rate, the overall cost of cancer care in 2021 is estimated to exceed \$147 billion.^{10,18,19} In July 2017, the FDA approved tisagenlecleucel-T for children and young adults with relapsed or refractory B-cell acute lymphoblastic leukemia (ALL). This was the first gene therapy in the US and it will cost patients \$475,000 as a one-time treatment.^{20,21} Such high prices and spending on cancer therapies come with significant “financial toxicity,” both to individual patients and to society.^{22,23} Stakeholders and society at large experience great financial pressure as the cost of treating cancer reaches unprecedented heights.^{24,25} This prompted a position statement from the American Society of Clinical Oncology (ASCO) that recommended that the affordability of cancer drugs be addressed, and it provided a number of key strategies to reduce antineoplastic expenditures.²⁶ To assess the effectiveness of the ASCO strategies and other programs to control antineoplastic costs, it is important to identify and describe the actual and current trends in antineoplastic expenditures in the US - both as a whole and within specific distribution channels. Moreover, while it is true that price increases have occurred in other drug classes, it is not clear how the rate of growth in expenditures over time has differed between traditional antineoplastic drugs and biologics. Therefore, the purpose of this study was to describe antineoplastic expenditures by year and healthcare sector in the US. We also sought to identify major contributors to changes in injectable antineoplastic expenditures specifically within the clinics and hospitals because these channels contribute to more than two-thirds of total antineoplastic expenditures.²⁷

METHODS:

We conducted an analysis of trends in expenditures for antineoplastic drugs for the period January 1, 2011 to December 31, 2016. Data for this analysis were obtained from the IQVIA (previously QuintilesIMS and IMS Health) National Sales Perspectives (NSP) database. The NSP is a statistically valid audit that projects 100% of the purchases in every major class of trade and distribution channel for prescription pharmaceuticals, nonprescription products, and select self-administered diagnostic products in the US, measuring both unit volume and invoice dollars. It is derived from annual transactions from pharmaceutical manufacturers to wholesaler distribution centers for sales to nonfederal hospitals, clinics, retail pharmacies, mail-service pharmacies, home health facilities, long-term-care outlets, and other entities. These transactions account for 340B discounts which are factored into the total expenditures.

Antineoplastic agents were categorized as either “biologics” or “drugs”, based on their approval pathways (i.e., through the 505(b)(2) New Drug Application or the 351(k) Biologics License Application). We evaluated overall antineoplastic expenditures within various health care sectors, which were aggregated into retail pharmacies, mail-order pharmacies, clinics, non-federal hospitals, long-term care, staff-model health maintenance organizations (HMOs), home health care, federal facilities, and other. Definitions for each health care sector are provided in Table 1. We subsequently evaluated trends in expenditures of specific products within the clinic and non-federal

hospital expenditures, and limited our analysis to include only injectable products, since these are the primary agents dispensed within clinics and hospitals.

Actual expenditures were totaled by health care sector and calendar year, and then adjusted for US medical-cost inflation (part of the overall consumer price index [CPI]) to 2016 dollars. Growth was calculated as the percentage increase from the previous year. According to the categories listed above, expenditures over time per sector were examined graphically. Descriptive statistical analysis was used to characterize the data.

RESULTS:

Total expenditure of antineoplastic agents across all channels within the US grew from \$26.8 billion in 2011 to \$42.1 billion in 2016 as shown in Table 1. Spending on antineoplastic agents increased 12.2% in 2016 compared to the previous year. The largest growth in the time period observed occurred in 2015 (15.6% increase compared with 2014). The smallest growth in spending was seen in 2012 (0.4% compared with 2011).

Annual expenditures of antineoplastic agents from 2011 to 2016 across each of the various sectors are also described in Table 1. Although staff-model HMOs saw the largest increase in antineoplastic expenditures from 2011-2016, with an average increase of 26.5% compared with the previous year, expenditures within the HMO sector are considerably lower than the other channels and comprises only 1% of the

total expenditures of antineoplastic agents. Mail-order pharmacies experienced the second largest growth in antineoplastic expenditures, with an average annual increase of 23.7% compared with the previous year while representing more than 20% of the total expenditures of antineoplastic agents. All the sectors saw a net increase in antineoplastic expenditures over the study period except for federal facilities (-17.2%) and long-term care (-5.5%).

The distribution of annual antineoplastic drug expenditures across each of the various healthcare sectors is shown in Figure 1. Clinics accounted for the largest portion of total antineoplastic expenditures (ranging from \$14.1 to \$21.1 billion and 47.7% to 54.5% of total antineoplastic expenditures), followed by mail-order pharmacies (ranging from \$3.9 to \$11.2 billion and 14.5% to 25.6% of total antineoplastic expenditures), non-federal hospitals (ranging from \$4.6 to \$6.1 billion and 16.2% to 17.5% of total antineoplastic expenditures) then retail pharmacies (ranging from \$2.4 to \$2.6 billion and 7.5% to 9.7% of total antineoplastic expenditures). The remaining sectors (long-term care, home health care, and other) accounted for less than 2% of total annual antineoplastic drug expenditures.

Significant fluctuations in distribution of total antineoplastic drug expenditures were seen in clinics, mail-order pharmacies, staff-model HMOs, and federal facilities. Clinics saw a consistent decline in its proportion of total antineoplastic drug antineoplastic drug expenditures (54.5% in 2011 to 50.1% in 2016), although the dollar amount of expenditures increased (\$14.1 billion in 2011 to \$21.1 billion in 2016). Throughout the

2011 to 2016 period, over 2/3 of antineoplastic drug expenditures remained within clinics and non-federal hospitals.

A visual comparison of expenditures of the top-selling agents considered to be traditional antineoplastic drugs, older antineoplastic biologics and newer antineoplastic biologics in hospitals and clinics is shown in Figure 2. The three antineoplastic agents that saw the largest decrease in expenditures from 2011 to 2016 in hospitals and clinics were traditional cytotoxic drugs that became generic during the study period: oxaliplatin (\$1.6 billion in 2011 to \$50 million in 2016, a 97% decrease), docetaxel (\$1.0 billion in 2011 to \$0.1 billion in 2016, an 89% decrease) and gemcitabine (\$0.4 billion in 2011 to \$36.8 million in 2016, a 92% decrease). The three antineoplastic drugs that maintained the largest expenditures from 2011 to 2016 in hospitals and clinics were older biologics: rituximab (average annual expenditure of \$3.5 billion), bevacizumab (average annual expenditure of \$2.9 billion) and trastuzumab (average annual expenditure of \$2.2 billion). The three antineoplastic drugs that saw the largest growth in expenditures from its first full year on the market to 2016 in hospitals and clinics were newer biologics: nivolumab (\$0.8 billion in 2015 to \$2.6 billion in 2016, a 238% increase), pertuzumab (\$0.2 billion in 2013 to \$0.9 billion in 2016, an 80% increase) and pembrolizumab (\$0.4 billion in 2015 to \$0.7 billion in 2016, an 84% increase).

DISCUSSION:

Our findings are that antineoplastic expenditures in the US have increased consistently from \$26.8 billion in 2011 (when the great recession was nearing its end) to \$42.1 billion in 2016, and that more recent increases (from 2014 to 2016, after the recession had resolved) were even more significant with an average annual increase of 13.7% compared to the previous year. Since 2011, total drug expenditures (including antineoplastics and all other drugs) across the US increased from \$328.4 billion (in 2011) to \$448.2 billion (in 2016). Antineoplastic expenditures represented 7% of total US drug expenditures in 2011 and rose to 9.4% in 2016.^{8,28} As reported by Express Scripts, the steep rise in 2016 antineoplastic drug spending can be attributed to increases in unit costs (11.9%) and utilization (9.6%).^{29,30}

The reasons for growth in cancer drug expenditures include technology advancements, rising prices, changing patient demographics, and changes in duration of therapy.

Technology advancements contribute towards the surge of new cancer therapies being approved, whereby most are targeted small molecules or targeted biologics, rather than traditional cytotoxic chemotherapy. Accordingly, these novel agents are more expensive than traditional cytotoxic therapies on a price per month or price per course basis. The aging population and advances in early detection have increased the incidence of cancer and subsequent use of antineoplastic therapy. Further, modern treatments have led to improvements in overall survival, resulting in longer treatment durations, thereby increasing drug expenditures.^{1,9,10,31,32}

Many of the newer cancer treatments are oral. In fact, we found a consistent increase in antineoplastic spending (23.7% average annual increase) in specialty and mail-order pharmacies from 2011 to 2016. A major driver is the growing shift from injectable to oral anticancer drugs.^{1,9,10,33} These newer and more expensive oral antineoplastic agents come with many advantages, but still exhibit poor adherence in a large proportion of patients.³⁴⁻³⁶ The use of specialty pharmacy drug programs have shown promise in improving adherence, and thus, payers are shifting utilization from high cost outpatient settings to lower cost community oncology settings. While this may further increase drug expenditures, total healthcare utilization and costs may decrease.^{37,38}

In addition to oral anticancer treatments, there has been high growth in the development of biologics. Targeted biologics made up 21% of the late phase oncology pipeline in 2006 and 43% in 2016. The strong clinical profile of the newer immuno-oncology agents has led to their rapid uptake and expanded use across multiple cancer types.¹⁰ We found that older biologics (rituximab, bevacizumab and trastuzumab) accounted for the highest antineoplastic expenditures in hospitals and clinics and remained that way from 2011 to 2016, while newer biologics (nivolumab, pertuzumab and pembrolizumab) saw exponential increases in expenditures.

These trends in expenditures indicate the growing and urgent need for expenditure and price reduction strategies. Biosimilars can help to moderate the expenditures of costly, older biologics and may off-set the increase in expenditures for the newer generation of

immuno-oncology drugs. For our study period of 2011-2016, there were no biosimilars approved for the active treatment of cancer in the United States. While there exists a significant number of barriers to entry for biosimilars in the US, there is still great potential for reducing biologic expenditures, as seen in Europe; they are priced approximately 30% less than their reference products.^{39,40} If this 30% discount is applied to the 2016 top three antineoplastic biologics in US clinics and hospitals (rituximab, bevacizumab and nivolumab), our healthcare system would save \$2.8 billion.

Another cost control strategy that has recently been the center of discussion is the promotion of value-based coverage decisions and/or value-based pricing. Groups such as ASCO, National Comprehensive Cancer Network (NCCN), Memorial Sloan Kettering Cancer Center (MSKCC), and Institute for Clinical and Economic Review (ICER) developed frameworks to help patients, manufacturers, providers and payers assess the value of treatments.⁴¹⁻⁴⁴ However, there exist many inherent complexities in assessing the value of treatments, including, but not limited to, an absence of any distinct theoretical basis to measure value and any empirical analyses regarding how stakeholders should make decisions based on these value metrics. Given the limitations listed above, stakeholders are being cautious in strictly promoting value-based policies.⁴⁵

Without shifting towards a value-based approach, insurance companies and payers have limited options to exert downward pressure on drug expenditures. Historical strategies used by private payers and pharmacy benefits managers revolve around

utilization management, including formulary tiers and mandatory prior authorizations.⁴⁶ However, for the first time, CVS Health excluded brand name cancer drugs, including those for imatinib and enzalutamide, from its formulary.⁴⁷ This strategy is controversial because they may restrict access to life-saving or extending treatments.⁴⁸ Another proposed strategy is to allow the largest payer for oncology drugs, the Centers for Medicare and Medicaid Services (CMS), to negotiate drug prices - a practice that is currently not allowed by law.⁴⁹⁻⁵¹ The CMS Innovation Center is currently developing the Oncology Care Model (OCM), which seeks to provide higher quality care at a lower cost. Programs participating in OCM are incentivized to implement evidence-based clinical pathways to promote the utilization of the most cost-effective drug therapies. As recognized by a recent ASCO Policy Statement, clinical pathways are also increasingly used by large payers to reduce variation and control drug costs.⁵²

Regardless of the future approaches taken, the information presented in our study serves as a baseline measure of actual transaction costs associated with antineoplastics by healthcare sector in the United States. Results of this analysis may be useful in informing decision among healthcare policy makers and healthcare providers, and for monitoring the impact of efforts to contain costs. Although other studies that examine antineoplastic expenditures exist, they are either projection based or focus on subpopulations or subgroups of antineoplastic agents.^{31,53} With rising antineoplastic expenditures and utilization of specialty and mail order pharmacies, future analyses should focus on expenditures within these channels.

There are several limitations to our analysis that should be considered when interpreting these results. The dataset used in this analysis captures wholesaler purchases and is not reflective of what is paid by patients or insurance companies. The NSP database is continually updated and analyses may lead to slightly different results depending on when it is accessed (for this analysis, it was accessed on February 1, 2017). Another limitation is that expenditure data is lacking from the Veterans Affairs (VA) system starting in the calendar year of 2014. This absence of this information affects expenditures reported in federal facilities, as shown in Table 1 and, to a lesser extent, total expenditures across all sectors. A recent report to Congress for the Fiscal Year 2017 of the TRICARE program (which includes the VA) indicates that spending on oncological agents increased by 41% from 2014 to 2016.⁵⁴ Last, there is potential for misclassification of expenditures by sector if the class of trade on record of the purchasing pharmacy was incorrectly documented. Though this is likely minimal it could lead to inaccuracies in the results by sector.

CONCLUSION:

Antineoplastic expenditures are expected to increase due to continuing development and approval of costly cancer therapies and an aging population. Payers should carefully consider the implications of cost containment and utilization management strategies so as not to restrict access to life-saving treatments or disrupt innovation in

oncology research. Policies should focus on ensuring safe and appropriate use of antineoplastics while balancing long term costs associated with cancer.

Figure 1 Legend.

% - Percent of Total Antineoplastic Agent Expenditures

\$ - Thousands of US Dollars

Figure 2 Legend.

\$ - Thousands of US Dollars

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